

TENT COOPERATION TREATY

PCT

NOTIFICATION OF THE RECORDING OF A CHANGE

(PCT Rule 92bis.1 and
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

HEIJLEK, Edward, J.
Senniger, Powers, Leavitt & Roedel
One Metropolitan Square
16th Floor
St. Louis, MI 63102
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year) 22 November 2001 (22.11.01)	
Applicant's or agent's file reference 3203/1/PCT	IMPORTANT NOTIFICATION
International application No. PCT/US00/09806	International filing date (day/month/year) 17 May 2000 (17.05.00)

1. The following indications appeared on record concerning:

☒ the applicant
 ☐ the inventor
 ☐ the agent
 ☐ the common representative

Name and Address

MONSANTO COMPANY
P.O. Box 5110
Chicago, IL 60680-5110
United States of America
Chicago, IL 60680-5110
United States of America

State of Nationality

US

State of Residence

US

Telephone No.

Facsimile No.

Teleprinter No.

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

☐ the person
 ☒ the name
 ☐ the address
 ☐ the nationality
 ☐ the residence

Name and Address

PHARMACIA CORPORATION
P.O. Box 5110
Chicago, IL 60680-5110
United States of America
St. Louis, MI 63102
United States of America

State of Nationality

US

State of Residence

US

Telephone No.

Facsimile No.

Teleprinter No.

3. Further observations, if necessary:

4. A copy of this notification has been sent to:

☒ the receiving Office
 ☐ the designated Offices concerned
☐ the International Searching Authority
 ☒ the elected Offices concerned
☐ the International Preliminary Examining Authority
 ☐ other:

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer <p style="text-align: center;">Beatriz LARGO</p> Telephone No.: (41-22) 338.83.38
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P. ENT COOPERATION TREA

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Commissioner
 US Department of Commerce
 United States Patent and Trademark
 Office, PCT
 2011 South Clark Place Room
 CP2/5C24
 Arlington, VA 22202
 ETATS-UNIS D'AMERIQUE
 in its capacity as elected Office

Date of mailing (day/month/year) 06 February 2001 (06.02.01)	
International application No. PCT/US00/09806	Applicant's or agent's file reference 3203/1/PCT
International filing date (day/month/year) 17 May 2000 (17.05.00)	Priority date (day/month/year) 19 May 1999 (19.05.99)
Applicant SOUTH, Michael, S. et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

18 December 2000 (18.12.00)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Claudio Borton Telephone No.: (41-22) 338.83.38
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PATENT COOPERATION TREATY

PCT

REC'D 31 AUG 2001

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

14

Applicant's or agent's file reference 11289/kö	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US00/09806	International filing date (day/month/year) 17/05/2000	Priority date (day/month/year) 19/05/1999
International Patent Classification (IPC) or national classification and IPC C07D239/46		
Applicant MONSANTO COMPANY et al.		



- This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
- This REPORT consists of a total of 7 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

 These annexes consist of a total of sheets.

- This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☒ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand 18/12/2000	Date of completion of this report 29.08.2001
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Mathys, E Telephone No. +49 89 2399 8596 

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US00/09806

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, pages:

1-177 as originally filed

Claims, No.:

1-50 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US00/09806

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 40-49.

because:

☒ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims 1-50
	No: Claims
Inventive step (IS)	Yes: Claims
	No: Claims 1-50
Industrial applicability (IA)	Yes: Claims 1-39,50

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/US00/09806

No: Claims

2. Citations and explanations
see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

ITEM III

Claims 40-49 relate to subject matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT.

Consequently, no opinion will be formulated with respect to the industrial applicability of the subject matter of these claims (see Article 34(4)(a)(i) PCT (see also ITEM V).

ITEM V

Novelty

The present compounds differ from the compounds disclosed by (D1) US-A-5 441 960 and (D2) WO-96/33974 in the arrangement of the structural elements of the N-substituent.

Inventive Step

The problem underlying the present subject matter was the provision of further compounds inhibiting serine proteases of the coagulation cascade.

From compounds having the same utility disclosed by D1 and D2 the present ones differ in the arrangement of the structural elements of the N-substituent. This arrangement is, however, known from e.g. (D3) WO-A-97/01338 and (D4) WO-A-99/11267 (both documents cited in your application PCT/US00/08220) for corresponding pyridinone and pyrazinone derivatives. It is therefore considered to have been obvious to solve the problem by replacing the N-substituent of compounds according to D1 and D2 by such ones known from D3 and D4 or the other way round by replacing in compounds according to D3 and D4 the pyridinone respectively pyrazinone by a similar azacycle known in the art, as pyrimidinone from D1 and D2.

Accordingly, the present subject matter does not fulfil the requirements of Article 33(3) of the PCT.

The above obviousness objection could be overcome if it were shown that present compounds exhibit unexpected properties (i.e. unexpectedly solve a problem not yet solved) when compared to the structurally closest related compounds known from the above mentioned state of the art.

Property establishing an inventive step must then extend to the whole of the scope

claimed. It is pointed out in this respect that an eventual solution of a problem establishing an inventive step based on the few present compounds having been shown to have an activity (see present description, Table 2 on page 176, for compounds wherein [SPEC0830], M, K, E⁰, and Y⁰ are always -NH-, -CH-, -CH₂-, -CONH- respectively amidinobenzyl, B is phenyl, isopropyl or cyclobutyl, A is -CH₂SO₂- or a bond and R² is phenyl, aminophenyl or pyridyl) could not at all imply that substantially all claimed alternatives to these working examples would also result in compounds solving said problem, since the best part of the listed myriad alternative substituents are not known in the art as obvious equivalents to the substantiated ones, i.e. an eventual inventive step could only be acknowledged for a scope representing a reasonable generalisation of the compounds shown to be a solution to the problem underlying the invention.

Industrial Applicability

For the assessment of present claims 40 to 49 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment (as present claim 50).

ITEM VII

The description does not mention the relevant background represented by the above cited documents as required by Rule 5.1(a)(ii) and (iii) PCT.

ITEM VIII

The drafting of the claims is not clear and concise as required by Article 6 PCT. In deciding this matter, regard has also to be had to the interest of the relevant public, since patents should not be allowed to erect a legal maze or smoke screen in front of potential users of the inventions to which they lay claim. Patent claims, taken singly as

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US00/09806

well as in totality, must be clear and concise in order to enable such potential users to ascertain, without undue burden, let alone recourse to litigation, whether their planned commercial use is likely to infringe the patent monopoly. Having to construe the present 50 claims with all their provisos and alternatives on more than 100 pages, and to form a valid and commercially useful opinion on whether or not any one of them could prevent or hinder the commercial activities must in the nature of things impose a severe and totally undue burden on the public. It follows that the present application as it stands falls foul of the clear provision not only of Rule 13(4) but also of Article 6 PCT.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 00/09806

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07D239/46 C07D253/06 C07D401/04 C07D417/12 A61K31/505
A61P9/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07D A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 441 960 A (P.R. BERNSTEIN) 15 August 1995 (1995-08-15) column 1 - column 20; claims	1, 8, 16, 24, 32-34, 38-41
A	WO 96 33974 A (THE GREEN CROSS CORPORATION) 31 October 1996 (1996-10-31) page 0; claims	1, 8, 16, 24, 32-34, 38-41

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

22 September 2000

Date of mailing of the international search report

29/09/2000

Name and mailing address of the ISA

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Authorized officer

Francois, J

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/09806

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 5441960	A	15-08-1995	AU 3959593 A	18-11-1993
			CA 2133659 A	28-10-1993
			DE 69311804 D	31-07-1997
			DE 69311804 T	27-11-1997
			EP 0636141 A	01-02-1995
			FI 944804 A	12-10-1994
			WO 9321210 A	28-10-1993
			HU 68402 A	28-06-1995
			JP 7505876 T	29-06-1995
			NO 943911 A	14-10-1994
			ZA 9302696 A	27-10-1993
WO 9633974	A	31-10-1996	CA 2219364 A	31-10-1996
			EP 0826671 A	04-03-1998
			US 5948785 A	07-09-1999